Some of their descendants do so to this day, and, among them, a genealogy could well trace to a single ancestral couple. With few exceptions, their surnames are different from those of the Acadian founders. Even the exceptions should prove no problem to define in careful genealogical studies.

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Reply to Thurmon

To the Editor:

Dr. Thurmon points out the many pitfalls inherent in collecting and interpreting genealogical data. We took into account such confounding factors as nonpaternity and undocumented relationships when analyzing our pedigrees, and we believe that entry of the Tay-Sachs disease (TSD) exon 11 insertion allele into the Cajun population after the early 19th century is inconsistent with the available genealogical data.

Dr. Thurmon's work demonstrates convincingly that the current population of southwest Louisiana is very closely related, and he is correct that our pedigrees are incomplete. We purposely eliminated from our study those lines of the families which we demonstrated by enzyme and molecular analysis not to carry the insertion allele. We were fortunate enough to be able to test family members two to four generations removed from the probands and were able to eliminate $^1/_2$–$^7/_8$ of the individuals from each pedigree in our study. What information we have on the excluded branches of our pedigrees suggests that there are indeed multiple common ancestors among these families. However, these other relationships are not informative as to the origin of the insertion allele.

Not all of the relatives of the insertion carriers were French Acadian, but most were, and all of the families in our study consider themselves to be members of the Cajun population. We determined French Acadian ancestry either by surname or by the identification of ancestors who lived in Acadia. In addition to the Acadians, southwest Louisiana was home to a German settlement established in 1717 and referred to as the "German Coast." Histories of this settlement state that Jews were among the German immigrants, but, as Dr. Thurmon points out, there is no documentation of this (Deiler 1909). When we began our genealogical work it seemed likely that the origin of the insertion allele would be among these German settlers. However, we have found no evidence to support a "German" origin of this allele. One of the obligate carriers in our study does not have any German relatives in his TSD carrier lines. As for the German relatives of the other obligate carriers, one German couple was found to be common only to three of the seven obligate carriers through carrier lines. Since the TSD carrier frequency among Jews is increased, it is possible that more than one unrelated family carrying this allele came to southwest Louisiana, although there is no evidence that there were many Jewish families in this early German community. Other genetic disorders increased in the Jewish population, such as Gaucher disease, are not reported in the Cajun population to suggest any large influx of Jewish alleles. If the origin of this allele is a single Jewish founder who is unrecognized because of a case of nonpaternity, then a common ancestral couple, albeit the wrong ancestral couple, still will be found. The timing of the entry of the TSD allele would be correct, though the geographic origin of the allele may not.

The conclusions of our study are supported by our data even after consideration of the possible confounding factors which Dr. Thurmon raises: namely, that (*a*) our pedigrees indicate that the insertion allele has been in southwest Louisiana at least since 1850 and probably since the founding of the Cajun community, and (*b*) founder effect is responsible, in part, for the increased occurrence of TSD in the Cajun community.

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The Designation of Mutations

To the Editor:

Many different conventions are used for the primary designation of mutations. Commonly, the amino acid change that has been deduced from the nucleotide substitution is employed, but often the cDNA number, the genomic number, or even a "nickname" based on a restriction site or a patient's name has been used. These notations are not, of course, mutually exclusive, and several of them are used in first describing a mutation. However, when the existence of a mutation becomes well established, it usually acquires a designation that is used exclusively, and that common name is the one to which I refer here.

An ideal nomenclature would be one that is entirely unambiguous. One might hope that a geneticist of the year 2493 could pick up a 1993 copy of *The American Journal of Human Genetics* and quickly understand, from the designation of a mutation and without extensive study of other sources, the location of a nucleotide change. However, the complexity of the genome and its functions is such that a perfect nomenclature is unachievable.

Amino acid–based mutation designation.—Surely a convention based on the amino acid change, embraced by so many geneticists, must have something to commend it. And so it does. One reason for the use of amino acid–based designations is the historical fact that a number of proteins, most notably hemoglobin, were sequenced at the protein level even before the DNA code was known. This, quite understandably, established a tradition from which it has sometimes been difficult to break. Another major reason for the use of this nomenclature seems to be the wish to divine the change in the gene product brought about by the mutation. Commendable as it may be, the idea that this can be achieved is often an illusion. Certainly a change to a stop codon near the amino terminus of the protein tells us much about the effect of the mutation. Knowing that a change in the nucleotide sequence does not change an amino acid is also useful, although the usual conjecture that such a mutation is "neutral" may in the future sometimes prove to be incorrect. It is entirely possible that some such mutations may exert an effect either because of their effect on the stability or translatability of the message or because of the abundance of the needed tRNA. Between these extremes, the data often do not reveal much about the effect of the mutation on the protein, although this may change with advances in understanding of protein structure.

There are, however, are a number of compelling disadvantages intrinsic to the use of the amino acid mutation as the primary nomenclature for the designation of mutations:

1. It is more logical to report what we actually find, rather that what we deduce. Genes are not composed of amino acids but of purine and pyrimidine bases. In the vast majority of cases it is the base sequence that is determined in the laboratory. Moreover, the deduction is occasionally wrong. Notable is the fact that in glutathione peroxidase the UGA codes for selenium cysteine, not for a stop codon (Chambers and Harrison 1987), and that the putative β141-deleted leucine in hemoglobin Atlanta-Conventry has actually been changed posttranslationally to hydroxyleucine (Brennan et al. 1992). There is actually no mutation at this location at all. The mutation in the β-chain of hemoglobin E produces an amino acid substitution, but it also causes aberrant splicing.

2. Any good notation should be not only logical but also unambiguous. The amino acid notation for the description of mutations has a number of serious, glaring ambiguities.

a. At least three different starting points for the numbering of amino acids are employed. Is one to use the sequence of the primary translated product, or is one to use the processed proteins? Does the start methionine